REMARKS/ARGUMENTS

Status of the claims

Claims 5-10, 14 and 15 are pending. With this action, claim 13 is canceled and claims 5, 7-10, 14 and 15 are amended.

Support for the amended claims is found throughout the specification and claims as originally filed. Specific support for adenomatous polyposis coli (APC) is found, *e.g.*, in paragraph [02] of the published application US20060100418. Support for a polypeptide of with amino acids 860-2829 of SEQ ID NO:1 deleted is found, *e.g.*, in original claim 13 and paragraph [14]. Support for an protein having the N-terminal 859 amino acids of APC is found in paragraph [104]. In the interest of clarity, Applicants have changed the language of the claim to recite the existing residues (*i.e.*, 1-859), instead of the deleted ones. Support for a polypeptide with 95% or higher identity to a mutant APC is found, *e.g.*, in paragraph [43]. No new matter has been added.

Objections to the claims

The Examiner has objected to claim 13 as allegedly drawn to unelected subject matter, and claim 15 as allegedly in improper multiple dependent form. Claim 13 has been canceled and claim 15 is now dependent only on claim 5. As such, Applicants respectfully submit that the present claims comply with the formal requirements.

Rejections under 35 USC § 101

The Examiner has rejected the claims as allegedly being directed to non-statutory subject matter. Amended claims 5 and 15 are now drawn to an isolated polynucleotide, as suggested by the Examiner. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejections under 35 USC § 112, second paragraph

The Examiner has rejected claim 5 as allegedly indefinite for reciting "APC." As amended, claim 5 provides the definition for "APC," and thereby resolves the basis of the rejection.

The Examiner has rejected claims 8, 9, and 14 as allegedly unclear for reciting "derived from." The language is deleted in amended claim 14, thereby rendering the rejection moot for that claim. Claims 8 and 9 are amended to reflect that the claims encompass both cells isolated from a mammal or amphibian **and** cells that have been altered that were derived from a mammal or amphibian (see, *e.g.*, paragraph [62]).

Claim 15 has been rejected as allegedly indefinite for not including an upper limit on the number of amino acids that can be substituted, deleted, added, or inserted. As amended, claim 15 depends on claim 5, which requires that the protein be 95% identical to amino acids 1-859 of SEQ ID NO:1.

Claim 13 is canceled, thereby rendering that particular rejection moot. In view of the claim amendments and foregoing comments, Applicants respectfully request withdrawal of the rejections under 35 USC § 112, second paragraph.

Rejections under 35 USC § 112, first paragraph -- Enablement

The Examiner has rejected the claims as allegedly lacking enablement. In particular, the Examiner states that the specification does not reasonably provide enablement for a polynucleotide that encodes any mutant APC, and that a large quantity of experimentation is necessary to generate the infinite number of recited derivates. Applicants appreciate the Examiner's acknowledgment that the specification does enable a polynucleotide encoding a mutant APC consisting of SEQ ID NO:1 with a deletion of residues 860-2829.

The test of enablement set forth by the Federal Circuit is "whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *In re Wands*, 858 F.2d at 737 (Fed. Cir. 1988). As explained in the MPEP § 2164.01, the fact that experimentation is required

or complex does not necessarily make it undue if the art typically engages in such experimentation.

In an effort to expedite prosecution, claim 5, from which the remaining claims depend, is amended to recite an APC protein consisting of a sequence 95% identical (or higher) to amino acids 1-859 of SEQ ID NO:1. As amended, claim 5 is enabled by the specification. Methods of modifying a polynucleotide sequence to encode a modified protein were well-known at the time of the invention, for example, site directed mutagenesis (see paragraph [52]). The structure and function of APC proteins were well-known at the time of filing. Thus, a skilled artisan would understand where modifications could be made without upsetting the activity of the APC protein (see, *e.g.*, paragraphs [36], [37], and [104] for description of APC domains). The specification teaches methods of expressing protein-encoding polynucleotides in various cell types. Methods of screening for "piling up of cells" are provided, for example, in paragraph [45], paragraphs [87]- [89], and Examples 3 and 4.

Thus, a skilled practitioner would be able to design a polynucleotide described in the claims and express the polynucleotide using standard molecular biological techniques, such as those described in the present specification. The practitioner would be further enabled to determine whether the protein induces piling up of cells using the screening techniques described in the specification. Protein expression and screening techniques are routine in the field, and do not constitute undue experimentation. Accordingly, Applicants submit that the claims comply with the Enablement requirement under 35 USC § 112, first paragraph, and respectfully request withdrawal of the rejection.

Rejections under 35 USC § 112, first paragraph -- Written description

The Examiner has rejected the claims as allegedly lacking written description in the specification. According to the Examiner, the nucleic acids of the claims are only defined by a functional characteristic.

Again, in an effort to expedite prosecution, claim 5 is amended to describe an APC protein consisting of a sequence 95% identical (or higher) to amino acids 1-859 of SEQ ID NO:1 that induces piling up of cells.

Example 14 of The Synopsis of Application of Written Description Guidelines (http://www.uspto.gov/web/menu/written.pdf) provides an analysis of a claim with similar limitations to those recited in amended claim 5. The Office found that the exemplified claim complied with the Written Description requirement because the claim required the protein to have a similar structure (at least 95% identity to a representative sequence) and a particular activity. Importantly, the specification provided a representative sequence and an assay for determining the recited activity. The Office concluded that the claimed genus of proteins would not have substantial variation because they must have the specified activity, and determined that a skilled artisan would conclude that the applicant had possession of the claimed subject matter.

Amended claim 5 complies with the Written Description requirement, as set forth in the USPTO's Guidance Example. The claimed polynucleotide encodes a protein with 95% or higher identity to amino acids 1-859 of SEQ ID NO:1 (structure) that induces piling up of cells (function). These limitations ensure that claimed genus of polynucleotides would not vary substantially. Moreover, the specification provides the sequence of the protein in SEQ ID NO:1, and provides primers to generate a polynucleotide encoding amino acids 1-859 in SEQ ID NOs:4 and 5. The specification and Examples describe how to express such a polynucleotide and assay for activity.

Accordingly, a skilled practitioner would conclude that the present Applicants had possession of the attributes possessed by the claimed genus. As such, Applicants respectfully request withdrawal of the rejection under 35 USC § 112, first paragraph for Written Description.

Rejections under 35 USC § 102(b)

The Examiner has made a number of rejections under 35 USC § 102(b). These are addressed individually below.

As stated in the MPEP § 2131, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Amended claim 5 recites a protein consisting of 95% or higher identity to amino acids 1-859 of SEQ ID NO:1 that induces piling up of cells.

Mimori-Kiyosue

The Examiner has alleged that the disclosure of Mimori-Kiyosue anticipates the claims. Mimori-Kiyosue discloses full length Xenopus APC, as well as truncation mutants representing amino acids 1-2158 and 2159-2829 (Figure 1). The reference also discloses that mutations in APC are correlated with colorectal tumors (page 506, column 1, paragraph 2). The reference does not, however, disclose a polynucleotide encoding a polypeptide with 95% identity or higher to amino acids 1-859 of SEQ ID NO:1 that induces piling up of cells. Thus, the particular sequence and activity recited in claim 5 are not taught by Mimori-Kiyosue. Moreover, the reference does not suggest that a protein of 859 amino acids would have such an activity. Because the reference does not teach every element of the claims, it does not anticipate the claims. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 USC § 102 based on Mimori-Kiyosue.

Oshima

The Examiner has alleged that the claims are anticipated by Oshima. Oshima teaches a murine APC of 716 amino acids. The reference does not, however teach an APC protein with 95% identity or higher to amino acids 1-859 of SEQ ID NO:1. The truncated APC is only 716 amino acids, instead of 859. Further, the murine APC sequence is only 86% identical over amino acids 1-859 SEQ ID NO:1 (see **Ex. 1** for BLAST alignment). Thus, the reference does not anticipate every element of the claims. Nothing in Oshima suggests that an APC protein with 95% identity or higher to amino acids 1-859 of SEQ ID NO:1 would have the recited activity. Applicants respectfully request withdrawal of the anticipation rejection based on Oshima.

Smith

The Examiner has rejected the claims as allegedly anticipated by Smith. Smith teaches truncation mutants of human APC that are commonly found in familial adenomatous polyposis. The truncations represent 1309 and 1941 amino acid proteins. The human APC sequence is only 86% identical over amino acids 1-859 of SEQ ID NO:1 (see **Ex. 2** for BLAST alignment). In addition, the reference does not disclose the activity recited in claim 5. Smith does not suggest an APC truncation with 859 amino acids or suggest that it would have the

recited activity. Thus, Smith does not anticipate every element of the claims. Applicants respectfully request withdrawal of the anticipation rejections based on Smith.

Su

The Examiner rejected claims 5 and 15 as allegedly anticipated by Su. Su teaches a mutation in the murine APC gene that results in a truncation at amino acid 850. As noted above, the murine APC protein sequence is only 86% identical over amino acids 1-859 of SEQ ID NO:1 (see **Ex. 1**). Su does not suggest a Xenopus APC truncation with 859 amino acids with that induces piling up of cells. Accordingly, the reference does not anticipate every element of the claims. Applicants respectively request withdrawal of the rejections under 35 USC § 102(b) based on Su.

In summary, the references cited by the Examiner do not teach every element of the amended claims. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 USC § 102(b).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

/Kevin Bastian/

Kevin Bastian
Reg. No. 34,774

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments (Ex. 1 and 2)
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